

IN THE SEQUENCE LISTING:

Kindly enter the attached substitute Sequence Listing in place of the existing Sequence Listing.

REMARKS

In response to the Notice to Comply with Requirements for patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures, Applicants submit herewith a substitute Sequence Listing; a Statement to Support Filing and Submission in Accordance with 37 CFR 1.821-1.825; and a copy of the Notice to Comply.

Initially, Applicants note that the Examiner has withdrawn the prior rejection of the claims 1-13 and 20-24 under 35 U.S.C. §112, second paragraph. Paper No. 10 at page 2.

Applicants respectfully request reconsideration of the pending rejections and reexamination of the present application in light of the proposed amendments and the remarks detailed below.

Claims 1, 3-13 and 20-25 are pending in this application. Proposed amendments to Claim 1 are submitted herewith. The amendments to the claims are supported by the specification and original claims (*see* specification, *e.g.*, at page 5, lines 25-32). It is submitted that no new matter has been introduced by the present amendments and entry of the same is respectfully requested. Applicants note that claims 14-19 are withdrawn from further consideration as being drawn to a nonelected invention, as recited in page 1 of Paper No. 4 and claim 2 has been canceled (Paper No. 9 at page 1).

By these amendments, the Applicants do not acquiesce to the propriety of any of the Examiner's rejections and do not disclaim any subject matter to which the Applicants are entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 U.S.P.Q.2d 1865 (U.S. 1997); and *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 56 U.S.P.Q.2d 1865 (Fed. Cir. 2000).

Non-statutory Double Patenting

On page 2 of Paper No. 10, the Examiner maintained the provisional rejection of claims 5-8 and 10-22 under the judicially created doctrine of obviousness-type double patenting over claims 1-17, 24-43 and 50-69 of co-pending Application No. 09/285,658. It remains unknown what subject matter claimed and disclosed in the present application and co-pending application 09/285,658 will be deemed allowable; hence any statement regarding

this rejection made on Applicants' part would be premature. Hence, Applicants respectfully traverse this rejection, and request that this provisional rejection should be held in abeyance until subject matter is deemed allowable in each of the applications.

Rejection Under 35 U.S.C. § 112, second paragraph

In paragraph 5 (page 2) of Paper No. 10, the Examiner maintained the rejection of claims 1-13 and 20-24 under 35 U.S.C. § 112, second paragraph. Specifically, the Examiner stated that exponential amplification is not proportional amplification. Applicants respectfully traverse this rejection.

In rendering the rejection, the Examiner indicated that the term "proportional" is unclear. Paper No. 10, paragraph 5 at page 2. As used in the claimed method, the term "proportional" amplification refers to the amplification of nucleic acids having the same or constant ratio. That is, the proportional amplification methods of the present invention, as described in the specification, provide reproducible results sufficient to facilitate the measurement of quantitative as well as qualitative differences in nucleic acid expression in tested samples. *See specification, e.g., at page 10, lines 29-32.*

It is thus submitted that the claims meet the requirements of 35 USC § 112, second paragraph, and reconsideration and withdrawal of the present rejection is respectfully requested.

Rejection Under 35 U.S.C. § 102: Kwoh et al.

In paragraph 6 (page 2) of Paper No. 10, the Examiner maintained the rejection of claims 1-12 under 35 U.S.C. § 102(b) as being anticipated by Kwoh et al. The Examiner stated that the limitation of a "four enzyme mix" is not recited in the claims. Paper No. 10 at page 2. Applicants respectfully traverse this rejection.

In order to support anticipation under 35 U.S.C. § 102, each and every element of a claimed invention must be disclosed within a single prior art reference. *See In re Bond*, 15 USPQ2d 1896 (Fed. Cir. 1991).

As amended and claimed, the invention relates to a method for proportional amplification of a population of nucleic acids where the amplification occurs in a single reaction vessel comprising a four enzyme mix.

Kwoh et al. discloses a method of amplifying a single nucleic acid. However, Kwoh et al. does not teach or disclose the proportional amplification of a nucleic acid population nor the use of a four-enzyme mix in a single reaction vessel for the amplification steps.

Since the method of nucleic acid amplification described by Kwoh et al. does not disclose the proportional amplification of a population of nucleic acids nor the use of a four-enzyme mix, Kwoh et al. does not teach each and every limitation of the claimed invention. Therefore, the Examiner has failed to establish a proper rejection under 35 U.S.C. § 102 (b). Accordingly, Applicants respectfully request reconsideration and withdrawal of the present rejection.

Rejection Under 35 U.S.C. § 103(a): Kwoh et al., Goller et al., Compton et al., and Schnipelsky et al.

In paragraph 8 (page 3) of Paper No. 10, the Examiner maintained the rejection of claims 1, 13, and 20-24 under U.S.C. § 103(a) as unpatentable over Kwoh et al., in view of Goller et al., Compton, and Schnipelsky et al. Applicants respectfully traverse.

To properly maintain a rejection under 35 U.S.C. § 103, three conditions must be met. First, the prior art must have suggested to those of ordinary skill in the art that they should make the claimed composition or device or carry out the claimed process. Second, the prior art must also have revealed that in so making or carrying out, those of ordinary skill in the art would have a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be adequately founded in the prior art and not in the Applicant's disclosure. Finally, the prior art reference must teach or suggest all the claim limitations. *See In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

The Examiner stated that the limitations such as "a single reaction vessel" and "without organic extraction and precipitation" are not in the claim language. Paper No. 10 at page 3.

As amended, the invention relates to the proportional amplification of a nucleic acid population where the amplification occurs in a single reaction vessel comprising a four enzyme mix.

As discussed above, Kwoh et al. does not teach or suggest the proportional amplification of a nucleic acid population nor the use of a four-enzyme mix in a single reaction vessel for the amplification steps. Goller et al., Compton, and Schnipelsky et al. do not remedy the deficiencies of Kwoh et al. as they do not teach or suggest the proportional

amplification of a nucleic acid population nor the use of a four-enzyme mix in a single reaction vessel for the amplification steps. Therefore, the teachings of Kwoh et al. in combination with Goller et al., Compton, and Schnipelsky et al. do not teach or suggest the present invention and the requisite reasonable expectation of success is absent. Accordingly, Applicants respectfully request reconsideration and withdrawal of the present rejection.

Rejection Under 35 U.S.C. § 103(a): Kwoh et al. and Sooknanan et al.

In paragraph 14 of Paper No. 10 (pages 4-5), the Examiner rejected claim 25 under U.S.C. § 103(a) as unpatentable over Kwoh et al. as applied to claim 1, and further in view of Sooknanan et al.

To properly maintain a rejection under 35 U.S.C. § 103, three conditions must be met. First, the prior art must have suggested to those of ordinary skill in the art that they should make the claimed composition or device or carry out the claimed process. Second, the prior art must also have revealed that in so making or carrying out, those of ordinary skill in the art would have a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be adequately founded in the prior art and not in the Applicant's disclosure. Finally, the prior art reference must teach or suggest all the claim limitations. *See In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

As amended and claimed, the invention relates to the proportional amplification of a nucleic acid population where the amplification occurs in a single reaction vessel comprising a four enzyme mix. The Examiner stated that one of ordinary skill would have been motivated to combine the teachings of Kwoh et al. and Sooknanan et al. to make the instant invention with reasonable expectation of success because the method of Kwoh et al. provides efficiency of steps to quantitatively produce RNA for specific detection and the method of Sooknanan et al. is enhanced NASBA in which the number of steps is reduced and eliminates the addition of a promoter sequence to derived DNA. Paper No. 10 at page 5.

The method of Sooknanan et al. does not teach or suggest a method for the proportional amplification of a population of nucleic acids. In fact, the Sooknanan reference only relates to a method to amplify a specific nucleic acid sequence. The method as claimed in the present invention defines a method to amplify a population of nucleic acid sequences. In addition, Kwoh et al. does not teach or suggest the proportional amplification of a nucleic acid population. Therefore, the teachings of Kwoh et al. in combination with Sooknanan et al. do not teach or suggest the present invention and the requisite reasonable expectation of

success is absent. Accordingly, Applicants respectfully request reconsideration and withdrawal of the present rejection.

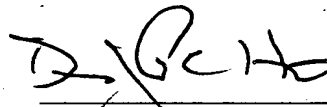
CONCLUSION

For the foregoing reasons, Applicants submit that all of the claims are in condition for allowance and Applicants respectfully request reexamination of the present application, reconsideration and withdrawal of the present rejections and entry of the amendments. Should there be any further matter requiring consideration, Examiner Tung is invited to contact the undersigned counsel.

If there are any further fees due in connection with the filing of the present reply, please charge the fees to undersigned's Deposit Account No. 50-1067. If a fee is required for an extension of time not accounted for, such an extension is requested and the fee should also be charged to undersigned's deposit account.

Respectfully submitted,

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Don J. Pelto
Reg. No. 33,754

McKenna & Cuneo LLP
1900 K Street NW
Washington, D.C. 20006-1108
Telephone: 202.496.7500
Facsimile: 202.496.7756

Claim Amendments, 27 June 2001

1. (Amended) A method for the amplification of nucleic acids, said method comprising:
 synthesizing double-stranded DNA from a single-stranded DNA population, and
 producing multiple copies of RNA from said double-stranded DNA,
wherein said amplification occurs in a single [phase] reaction vessel comprising a four
enzyme mix, and wherein said amplification is proportional.